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Synthesis and *In Vitro* Anti-Helicobacter and Anti-Staphylococcal Activities of Novel Diaryldisulfides and Diarylthiosulfonates

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Abstract

Arylthiols were reacted with acrylonitrile under basic conditions to form the corresponding aryl sulfides which were oxidised with sodium metaperiodate in aqueous methanol to yield 3-arylsulphonylpropanenitriles that upon thermolysis in refluxing toluene produced a mixture of diarylthiosulfonates and diaryldisulfides. The mixture of the two products was easily separated by flash chromatography and characterized spectroscopically. The diarylthiosulfonates and diaryldisulfides, garlic-like organosulfur compounds, were tested for their antimicrobial properties against *Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Helicobacter pylori* and had been found to have good activity against *S. aureus* and *H. pylori* with no activity against the other two organisms.

Keywords

Diarylthiosulfonates, Diaryldisulfides, *Helicobacter pylori*, Arylsulfenic Acids, Michael Reaction

1. Introduction

The medicinal properties of crushed garlic and onions are well recognized [1] [2]. The natural products in garlic responsible for the therapeutic actions are identified as the thiosulfinate esters alliin (S-allyl-L-cysteine sulfoxide) and allicin (di-allylthiosulfinate) (Figure 1) which have been reported to have a broad range of biological activities such as for example anti-inflammatory [1] and antibacterial [3] [4] actions.

In the laboratory synthetic versions of thiosulfinate esters have usually been made by either the oxidation of diaryldisulfides [5] [6] [7] [8] with peracids or by condensation of a sulfinyl chloride with a thiol in the presence of a tertiary

amine [8] [9] [10]. A third method which has been little used for making symmetrical diarylthiosulfonates involves the condensation of arylsulfenic acids generated *in situ* by thermolysis of arylsulfoxides possessing β -hydrogens. The β -elimination of sulfoxides to yield sulfenic acids and the condensation of sulfenic acids to form thiosulfinate esters are well documented in the literature [11] (Figure 2).

In our previously reported synthesis of phenylsulfinyl alkene derivatives by the Markovnikov addition of benzenesulfenic acid to terminal alkynes, generated *in situ* by thermolysis of 3-phenylsulfinylpropanenitrile [12] the diphenylthiosulfinate produced as a by-product was always disposed of. In this article, we report this synthetic strategy of making diarylthiosulfonates by condensation of arylsulfenic acids in the absence of any terminal alkynes as trapping agents.

The antimicrobial activity of garlic is mainly due to the thiosulfinate ester called allicin and is reported to be three times more effective on Gram-positive bacteria than Gram-negative ones [13]. The antibacterial activity of aqueous garlic extract against 16 *H. pylori* strains has been assessed and MIC₅₀ concentrations in the range 2 - 5 mg ml⁻¹ were able to inhibit the strains. In most cases, the inhibitory concentrations [4] were also bactericidal.

Helicobacter pylori and its clinical association with the development of peptic ulcers has led to the development of various chemotherapeutic agents to eliminate infection caused by this pathogen [14] [15] [16] [17] [18]. *H. pylori* is also implicated in the development of acute and chronic gastritis, gastric adenocarcinoma and gastric lymphoma (MALT), and has been classified as a class I carcinogen in humans and is a major contributing factor in the development of gastric cancer [19]. Infection with *H. pylori* is typically treated with a combination of clarithromycin, ampicillin and a proton pump inhibitor, but this triple therapy approach is costly [20]. The infection is eradicated in up to 90% of patients but side effects, poor compliance and the development of antimicrobial resistance are common causes of treatment failure [21]. *H. pylori* infection has been implicated with increased COX-2 expression in gastric antral mucosa for both NSAID users and non-users [22] [23] [24]. We have been engaged with the search for compounds with anti-*H. pylori* activity and have recently reported anti-*H. pylori* activity of novel quinoline-derived propionic acid esters [25]. In this paper, we report the synthesis and antimicrobial activities of a set of diaryl disulfides **6** and diaryl thiosulfonates **7**.

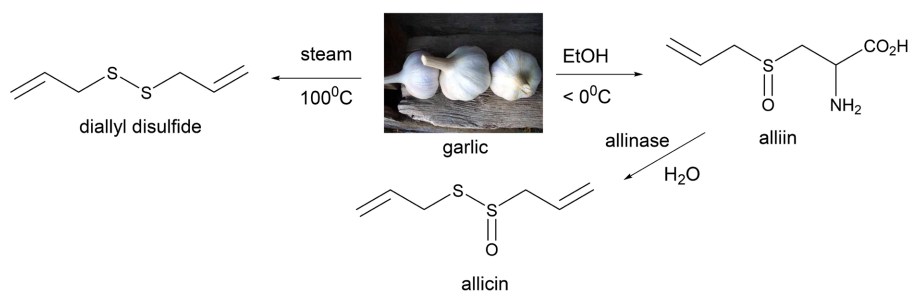


Figure 1. Enzymatic conversion of alliin into diallylthiosulfinate (allicin).

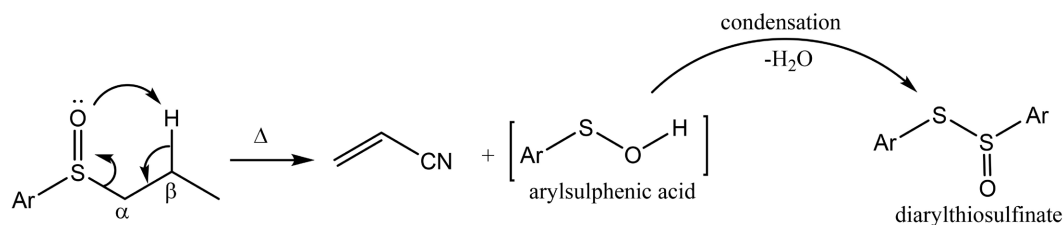


Figure 2. b-Elimination arylsulphoxides to produce sulphenic acids.

Staphylococcus aureus is a versatile pathogen that can cause a range of infectious diseases ranging from superficial skin infections to life-threatening septicaemia. The emergence of antibiotic-resistant strains of *S. aureus* including MRSA, VISA, LRSA and multi-drug resistant isolates has led to a great deal of interest in developing novel anti-staphylococcal agents [26] [27] [28].

Escherichia coli is a common commensal organism in the human gastrointestinal tract but it is also a significant pathogen that can cause a range of human infections including diarrheal diseases and urinary tract infections through wound infections and life-threatening ulcerative colitis and septicaemia [29] [30].

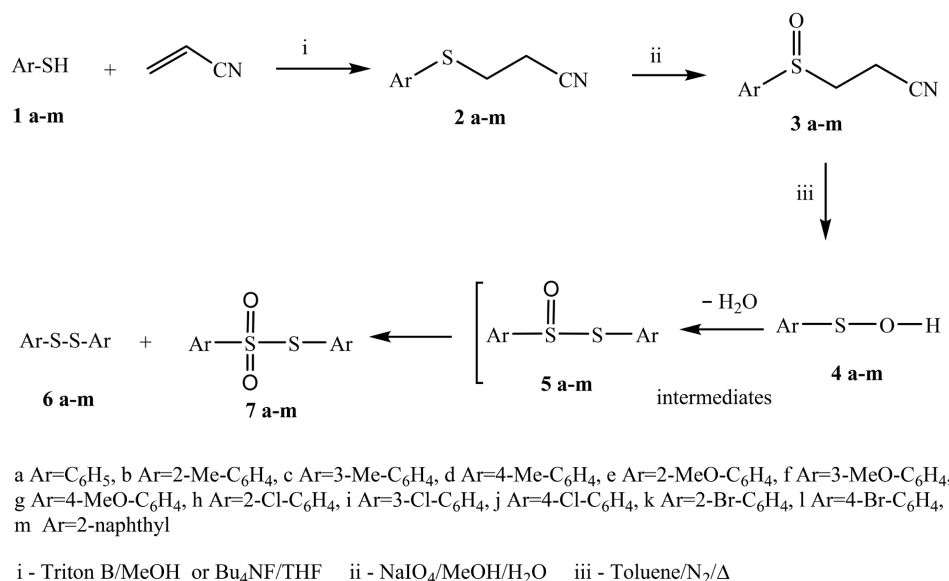
Due to the structural similarity of our synthetic compounds **6** and **7** to thiosulfinate esters found in garlic, we decided to investigate their preliminary antimicrobial activity against *Helicobacter pylori* and a Gram-positive bacterium, *Staphylococcus aureus* (including resistant strains of this species), and the Gram-negative bacterium, *Escherichia coli*.

2. Results and Discussion

2.1. Chemistry

Conjugate addition of thiolate anions to acrylonitrile furnished the arylsulfides **2a-i** and **2k-m** in excellent date yields (93% - 98%) with **2j** obtained in 82% yield. Sodium metaperiodate is a specific oxidising agent for converting sulfides into sulfoxides. Thus oxidation of the sulfides **2a-m** with one-molar equivalent of sodium metaperiodate in aqueous methanol yielded the corresponding sulfoxides **3a-m** which were isolated in good yields (63% - 89%) and characterised spectroscopically. The FTIR spectra showed the $>S=O$ absorbance at 1043 - 1093 cm^{-1} . Upon refluxing in toluene under nitrogen the sulfoxides **3a-m** thermolized to furnish the disulfides **6a-m** and diarylthiosulfonates **7a-m** as the only reaction products according to TLC analysis. The mixtures diaryldisulfides **6a-m** and diarylthiosulfonates **7a-m** were separated and isolated by flash chromatography (Scheme 1).

Our disappointment in not obtaining the anticipated diarylthiosulfonates **5** as reaction products was shown by subsequent literature search that described diarylthiosulfonates **5** to be thermally unstable compounds due to the weak S-S bond (bond strength ~ 35 kcal) [31]. Thermolysis of the sulfoxides **3** initially generates arylsulphenic acids **4** which by virtue of their high reactivity condense to



Scheme 1. Synthesis of 1-arylsulphanyl-2-cyanoethanes **3** and their thermolysis to form products **6** and **7**.

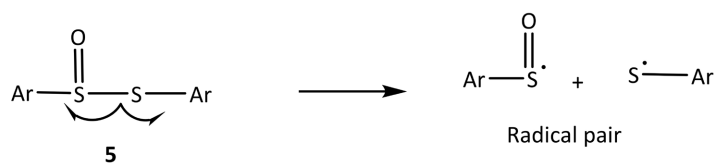
form diarylthiosulfonates **5** and water. Compounds of the formula RS(O)SR tend to be unstable and usually cannot be isolated. At the high temperature of the reaction the weak sulfinyl-sulfide S-S bond cleaves homolytically to generate radical pairs [32]. The recombination of arylsulfinyl radicals then produces the isolated symmetrical product **6** (Scheme 2).

The recombination of arylsulfinyl radicals did not produce any of the anticipated α,α' -diaryldisulfoxide **8** as reaction product [33] [34] but instead produced the thiosulfonate **7** as the isolated reaction product. The only evidence to date for the existence of stable α,α -disulfoxides has been provided by bridged bicyclic compound **9** [35].

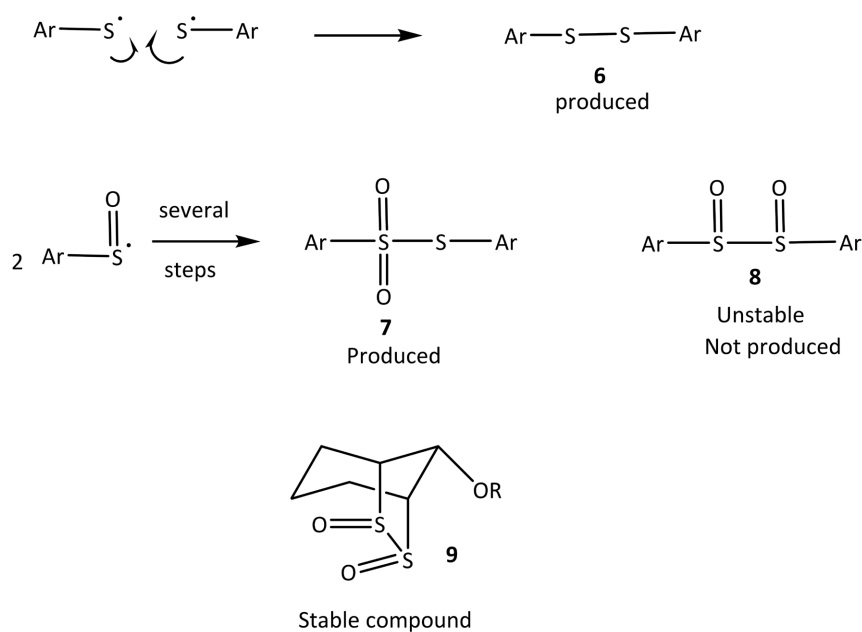
2.2. Microbiological Results and Discussion

An increase in resistance of bacteria and fungi towards currently available anti-bacterial and antifungal agents has resulted in a huge demand for the identification of novel antimicrobial agents. This is due to the rapid development of anti-microbial-resistant bacterial and fungal strains as well as a lack of new antimicrobial drugs that are effective against these resistant strains. Antimicrobial screening assays provide a robust method for the discovery of potential inhibitors of microbial growth. Due to the structural similarity of our synthetic compounds **6** and **7** to thiosulfonate esters found in garlic we decided to investigate their preliminary antimicrobial activity against *Helicobacter pylori* and a Gram-positive bacterium, *Staphylococcus aureus* (including resistant strains of this species, and the Gram-negative bacterium, *Escherichia coli*. The diarylthiosulfonates **7d**, **7h**, **7j**, **7k**, **7l** and **7m** and diaryldisulfides **6d**, **6h**, **6j**, **6k**, **6l** and **6m** were dissolved in 50% DMSO and tested for their antimicrobial activities using the broth microdilution method (Table 1).

Step 1: Formation of radical pairs



Step 2: Recombination to form reaction products isolated



Scheme 2. The disproportionation and recombination of thiol and arylsulfinyl radicals to form the products **7** and **8**.

Table 1. Antimicrobial activity of compounds **6a-f**, **6h**, **6j**, **6k-m** and **7b-e**, **7g-h**, **7j-l**.

Compound	MIC (µg/ml) <i>H. pylori</i> 3339	MIC (µg/ml) <i>H. pylori</i> 26695	MIC (µg/ml) <i>E. coli</i>	MIC (µg/ml) <i>S. aureus</i>
6a			>256	
6b	64	32	>256	64
6c	32	64		
6d	64	128		
6e	16	32	>256	>256
6f			>256	>256
6h	32	32	>256	4
6j	16	32	>256	16
6k	32	32	>256	8
6l	16	64	>256	16
6m	64	64		
7b	16	64	>256	32

Continued

7c	16	32		
7d		32	>256	16
7e	32	64	>256	128
7g	16	16	>256	32
7h	64	>128	>256	4
7j	16	64	>256	32
7k	16	32	>256	2
7l	32	32	>256	>256
Ampicillin	0.032	0.032	4	4
Ciprofloxacin	0.5	0.5	0.06	0.25
Tetracycline	1	1	1	1

Although there was no antimicrobial activity of any of the compounds against the Gram-negative pathogen *E. coli* there was some very promising effect on the common Gram-positive pathogen *S. aureus*. Compounds **6** and **7** were significantly inactive in antimicrobial activity against *E. coli* showing activity only at > 256 µg/mL but displayed modest activity against the other two organisms *H. pylori* 3339 and *S. aureus*. All the derivatives **6e**, **6j**, **6l**, **7b**, **7c**, **7g** and **6g** as a mixture, **7j** and **7k** have shown modest antimicrobial activity against *H. pylori* 3339 when compared with the standard anti-*Helicobacter* agents shown in **Table 1**. There is a noticeable common Structure-Activity Relationship (SAR) observed in inhibitory activity for the two different sets of compounds **6** and **7** on the *H. pylori* strain 3339. It was seen that when the aromatic rings in compounds **6** and **7** are *ortho*- and *para*-substituted with -OMe, -Cl and -Br groups the compounds tend to have the lowest concentration inhibitory effects overall. On the other hand some of the compounds **6** and **7** have shown modest to good antimicrobial activity against *S. aureus*. In particular the diaryldisulfides **6h**, **6k** and diarylthiosulfonates **7h** and **7k** gave the lowest inhibitory responses that are either equal or better than ampicillin. Thus, it is interesting to note that diarylthiosulfonate **7k** is the most active at 2 µg/mL whilst its counterpart diaryldisulfide **6k** inhibits at a somewhat higher concentration of 8 µg/mL. Similarly the 2-chloro derivatives of **6** and **7** showed good inhibitory action against *S. aureus* at 4 µg/mL. Thus, a noticeable structure-activity feature of the most promising four active compounds **6h**, **6k**, **7h** and **7k** is the presence of chloro- or bromo-groups in the 2-position of the aromatic rings. We conclude that for good inhibitory activity against *S. aureus* compounds **6** and **7** require of an *ortho*-substituted chlorine or bromine atoms as best candidates for further antibacterial studies.

3. Experimental

3.1. General Methods

Melting points are uncorrected and were determined on Stuart Scientific SMP3

apparatus. Infrared spectra were recorded with an ATI Mattson Genesis series FTIR spectrophotometer. ^1H NMR and ^{13}C NMR spectra were recorded in CDCl_3 using a Bruker AC 250 spectrometer operating at 250 and 62.9 MHz, respectively. Chemical shifts (δ) are in ppm downfield from Me_4Si as internal standard and J values are given in Hz. Mass spectra were recorded with EI-VG 7070E mass spectrometer. Accurate masses were determined on VG Autospec, EI mass spectrometer with magnetic sector instrument.

3.2. Typical Experimental Procedure for the Formation of Sulfides **2 a-m**

To a magnetically stirred solution of thiol **1** (0.10 mol) and acrylonitrile (20 ml, an excess) in THF (40 ml) at 0°C was added a solution of tetrabutylammonium fluoride in THF (2 ml) and the mixture was allowed to stir and come to room temperature overnight. The solvent was rotary evaporated and the residue extracted with DCM (160 ml). The organic solution was washed with 2M NaOH solution (2×40 ml) and water (50 ml) before being dried over MgSO_4 and evaporated to yield the crude sulfide **2** which according to TLC [1: 5 EtOAc-petrol] did not require any further purification. **2a** [12], **2b**: oil, 98% yield, IR ν 2248 (CN) cm^{-1} ; ^1H NMR δ 2.43 (3H, s, CH_3), 2.56 (2H, t, $J = 7.8$ Hz, SCH_2 -), 3.10 (2H, t, $J = 7.8$ Hz, $-\text{CH}_2\text{CN}$), 7.10 - 7.40 (4H, m, Ar); MS m/z 177 (M^+ , 73%), 137 ($\text{M}-\text{CH}_2\text{CN}$, 100%); **2c**: oil, 93% yield, IR ν 2248 (CN) cm^{-1} ; ^1H NMR δ 2.35 (3H, s, CH_3), 2.58 (2H, t, $J = 7.8$ Hz, SCH_2 -), 3.08 (2H, t, $J = 7.8$ Hz, $-\text{CH}_2\text{CN}$), 7.03 - 7.30 (4H, m, Ar); EIMS: m/z 177 (M^+ , 64%), 137 ($\text{M}-\text{CH}_2\text{CN}$, 100%); **2d**: oil, 93% yield, IR ν 2248 (CN) cm^{-1} ; ^1H NMR δ 2.37 (3H, s, CH_3), 2.55 (2H, t, $J = 7.8$ Hz, SCH_2 -), 3.10 (2H, t, $J = 7.8$ Hz, $-\text{CH}_2\text{CN}$), 7.15 (2H, d, $J = 7.5$ Hz, AB system Ar), 7.34 (2H, d, $J = 7.5$ Hz, AB system Ar); EIMS: m/z 177 (M^+ , 64%), 137 ($\text{M}-\text{CH}_2\text{CN}$, 100%); **2e**: oil, 98% yield, IR ν 2248 (CN) cm^{-1} ; ^1H NMR δ 2.58 (2H, t, $J = 7.8$ Hz, SCH_2 -), 3.11 (2H, t, $J = 7.8$ Hz, $-\text{CH}_2\text{CN}$), 3.90 (3H, s, OCH_3), 6.83 - 6.94 (2H, m, Ar); 7.23 - 7.40 (2H, m, Ar); EIMS: m/z 193 (M^+ , 100%), 153 ($\text{M}-\text{CH}_2\text{CN}$, 69%); **2f**: oil, 98% yield, IR ν 2248 (CN) cm^{-1} ; ^1H NMR δ 2.63 (2H, t, $J = 7.8$ Hz, SCH_2 -), 3.13 (2H, t, $J = 7.8$ Hz, $-\text{CH}_2\text{CN}$), 3.80 (3H, s, OCH_3), 6.80 (1H, d, $J = 7.5$ Hz, Ar H-4); 6.88 - 7.00 (2H, m, Ar); (1H, t, $J = 7.5$ Hz, Ar H-5); EIMS: m/z 193 (M^+ , 100%), 153 ($\text{M}-\text{CH}_2\text{CN}$, 68%), 140 ($\text{M}-\text{CH}_2\text{CH}_2\text{CN}$, 63%); **2g**: oil, 93% yield, IR ν 2248 (CN) cm^{-1} ; ^1H NMR δ 2.52 (2H, t, $J = 7.8$ Hz, SCH_2 -), 2.98 (2H, t, $J = 7.8$ Hz, $-\text{CH}_2\text{CN}$), 3.80 (3H, s, OCH_3), 6.87 (2H, d, $J = 7.5$ Hz, AB system Ar H-3 and H-5), 7.40 (2H, d, $J = 7.5$ Hz, AB system Ar H-2 and H-6); EIMS: m/z 193 (M^+ , 100%), 153 ($\text{M}-\text{CH}_2\text{CN}$, 77%), 140 ($\text{M}-\text{CH}_2\text{CH}_2\text{CN}$, 70%); **2h**: oil, 98% yield, IR ν 2252 (CN) cm^{-1} ; ^1H NMR δ 2.64 (2H, t, $J = 7.8$ Hz, SCH_2 -), 3.17 (2H, t, $J = 7.8$ Hz, $-\text{CH}_2\text{CN}$), 7.15 - 7.30 (2H, m, Ar); 7.35 - 7.45 (2H, m, Ar); EIMS: m/z 197.5 (M^+ , 52%), 157.5 ($\text{M}-\text{CH}_2\text{CN}$, 100%); **2i**: oil, 98% yield, IR ν 2252 (CN) cm^{-1} ; ^1H NMR δ 2.63 (2H, t, $J = 7.8$ Hz, SCH_2 -), 3.12 (2H, t, $J = 7.8$ Hz, $-\text{CH}_2\text{CN}$), 7.17 - 7.30 (3H, m, Ar), 7.37 (1H, s, Ar); EIMS: m/z 197.5 (M^+ , 60%), 157.5 ($\text{M}-\text{CH}_2\text{CN}$, 100%); **2j**: oil, 82% yield, IR ν 2243 (CN) cm^{-1} ; ^1H NMR δ 2.58 (2H, t, $J = 7.8$ Hz, SCH_2 -), 3.12 (2H, t, $J = 7.8$ Hz, $-\text{CH}_2\text{CN}$), 7.20

- 7.38 (4H, m, Ar); EIMS: m/z 197.5 (M^+ , 56%), 157.5 (M-CH₂CN, 100%); **2k**: oil, 98% yield, IR ν 2248 (CN) cm⁻¹; ¹HNMR δ 2.65 (2H, t, J = 7.8 Hz, SCH₂-), 3.18 (2H, t, J = 7.8 Hz, -CH₂CN), 7.05 - 7.18 (1H, m, Ar); 7.20 - 7.50 (2H, m, Ar), 7.52 - 7.67 (1H, m, Ar); EIMS: m/z 242 (M^+ , 37%), 202 (M-CH₂CN, 100%); **2l**: oil, 98% yield, IR ν 2243 (CN) cm⁻¹; ¹HNMR δ 2.57 (2H, t, J = 7.8 Hz, SCH₂-), 3.10 (2H, t, J = 7.8 Hz, -CH₂CN), 7.26 (2H, d, J = 7.5 Hz, AB system Ar), 7.45 (2H, d, J = 7.5 Hz, AB system Ar); EIMS: m/z 242 (M^+ , 48%), 202 (M-CH₂CN, 51%); **2m**: oil, 93% yield, IR ν 2248 (CN) cm⁻¹; ¹HNMR δ 2.60 (2H, t, J = 7.8 Hz, SCH₂-), 3.20 (2H, t, J = 7.8 Hz, -CH₂CN), 7.40 - 7.60 (3H, m, Ar); 7.72 - 7.95 (4H, m, Ar); EIMS: m/z 213 (M^+ , 49%), 202 (M-CH₂CN, 46%), 43 (100%).

Typical experimental procedure for the formation of 3-arylsulfinylpropanenitriles

3a-m:

To a vigorously stirred solution of sodium metaperiodate (0.0763 mol) in water (135 ml) at 0°C was quickly added a solution of the sulfide **2** (0.0763 mol) in methanol (135 ml) and the mixture was stirred for 22h and allowed to come to RT. The precipitated inorganic solid was filtered at the pump and the mother liquor extracted with DCM (3 × 200 ml). After washing with water (100 ml) the organic layer was dried (MgSO₄) and evaporated to yield the crude sulfoxide **3** which was purified by flash chromatography [2:3 ethyl acetate-petrol followed by ethyl acetate]. **3a** [12], **3b**: 82% yield, IR ν 2246 (CN), 1035, 1068 (>S=O) cm⁻¹; ¹H NMR δ 2.30 (3H, s, CH₃), 2.40 - 2.60 (1H, m, -CHCN), 2.75 - 2.93 (2H, m, -SO-CH₂-), 3.05 - 3.22 (1H, m, -CHCN), 7.10 - 7.25 (1H, m, Ar), 7.30 - 7.45 (2H, m, Ar), 7.67 - 7.80 (1H, m, Ar); EIMS: m/z 193 (M^+ , 29%), 140 (M-CH₂=CH-CN, 46%), 139 (M-CH₂CH₂CN, 60%), 77 (100%); HRMS: Found 193.0565. Calcd. for C₁₀H₁₁NOS 193.0561; **3c**: 85% yield, IR ν 2246 (CN), 1049, 1085 (>S=O) cm⁻¹; ¹H NMR δ 2.36 (3H, s, CH₃), 2.32 - 2.50 (1H, m, -CHCN), 2.72 - 2.95 (2H, m, -SO-CH₂-), 3.10 - 3.25 (1H, m, -CHCN), 7.20 - 7.40 (4H, m, Ar); EIMS: m/z 193 (M^+ , 14%), 140 (M-CH₂=CH-CN, 16%), 139 (M-CH₂CH₂CN, 67%), 66 (100%); HRMS: Found 193.0568. Calcd. for C₁₀H₁₁NOS 193.0561; **3d**: 76% yield, IR ν 2246 (CN), 1045, 1085 (>S=O) cm⁻¹; ¹H NMR δ 2.33 (3H, s, CH₃), 2.27 - 2.50 (1H, m, -CHCN), 2.70 - 2.95 (2H, m, -SO-CH₂-), 3.05 - 3.20 (1H, m, -CHCN), 7.30 (2H, d, J = 7.5 Hz, AB system Ar), 7.43 (2H, d, J = 7.5 Hz, AB system Ar); EIMS: m/z 193 (M^+ , 13%), 140 (M-CH₂=CH-CN, 23%), 139 (M-CH₂CH₂CN, 100%), 91 (43%); HRMS: Found 193.0557. Calcd. for C₁₀H₁₁NOS 193.0561; **3e**: 65% yield, IR ν 2246 (CN), 1039, 1068 (>S=O) cm⁻¹; ¹H NMR δ 2.25 - 2.45 (1H, m, -CHCN), 2.64 - 2.85 (1H, m, -SO-CH-), 2.97 - 3.13 (1H, m, -SOCH-), 3.15 - 3.34 (1H, m, -CHCN), 2.83 (3H, s, OCH₃), 6.86 (1H, d, J = 7.5 Hz, Ar), 7.10 (1H, t, J = 7.5 Hz, Ar), 7.43 (1H, t, J = 7.5 Hz, Ar), 7.60 (1H, d, J = 7.5 Hz, Ar); EIMS: m/z 209 (M^+ , 18%), 156 (M-CH₂=CH-CN, 44%), 155 (M-CH₂CH₂CN, 100%); HRMS: Found 209.0517. Calcd. for C₁₀H₁₁NO₂S 209.0510; **3f**: 89% yield, IR ν 2246 (CN), 1043 (>S=O) cm⁻¹; ¹H NMR δ 2.32 - 2.52 (1H, m, -CHCN), 2.67 - 2.94 (2H, m, -SO-CH₂-), 3.05 - 3.22 (1H, m, -CHCN), 2.75 (3H, s, OCH₃), 6.88 - 7.10 (3H, m, Ar), 7.28 - 7.43 (1H, t, J = 7.5 Hz, Ar); EIMS: m/z 209

(M^+ , 12%), 156 ($M\text{-CH}_2\text{=CH-CN}$, 18%), 155 ($M\text{-CH}_2\text{CH}_2\text{CN}$, 65%); HRMS: Found 209.0515. Calcd for $C_{10}H_{11}NO_2S$ 209.0510; **3g**: 89% yield, IR ν 2246 (CN), 1043, 1087 ($>S=O$) cm^{-1} ; ^1H NMR δ 2.38 - 2.53 (1H, m, -CHCN), 2.69 - 2.95 (2H, m, -SO-CH₂-), 3.03 - 3.17 (1H, m, -CHCN), 3.77 (3H, s, OCH₃), 6.97 (2H, d, J = 7.5 Hz, AB system Ar), 7.47 (2H, d, J = 7.5 Hz, AB system Ar); EIMS: m/z 209 (M^+ , 16%), 156 ($M\text{-CH}_2\text{=CH-CN}$, 45%), 155 ($M\text{-CH}_2\text{CH}_2\text{CN}$, 100%); HRMS: Found 209.0509. Calcd for $C_{10}H_{11}NO_2S$ 209.0510; **3h**: 86% yield, IR ν 2246 (CN), 1043, 1087 ($>S=O$) cm^{-1} ; ^1H NMR δ 2.38 - 2.40 (1H, m, -CHCN), 2.70 - 2.90 (1H, m, -SO-CH-), 3.00 - 3.18 (1H, m, -SO-CH-), 3.22 - 3.42 (1H, m, -CHCN), 7.30 - 7.60 (3H, m, Ar), 7.75 (1H, d, J = 7.5 Hz, Ar); EIMS: m/z 213.5 (M^+ , 38%), 160.5 ($M\text{-CH}_2\text{=CH-CN}$, 34%), 159.5 ($M\text{-CH}_2\text{-CH}_2\text{CN}$, 100%); HRMS: Found 213.00146. Calcd for C_9H_8NSCl 213.0015 (Cl^{35}); **3i**: 73% yield, IR ν 2246 (CN), 1051 ($>S=O$) cm^{-1} ; ^1H NMR δ 2.40 - 2.58 (1H, m, -CHCN), 2.70 - 2.98 (2H, m, -SO-CH₂-), 3.10 - 3.28 (1H, m, -CHCN), 7.33 - 7.47 (3H, m, Ar), 7.75 (1H, s, Ar); EIMS: m/z 213.5 (M^+ , 25%), 160.5 ($M\text{-CH}_2\text{=CH-CN}$, 30%), 159.5 ($M\text{-CH}_2\text{CH}_2\text{CN}$, 100%); HRMS: Found 213.0016. Calcd for C_9H_8NSCl 213.0015 (Cl^{35}); **3j**: 66% yield, IR ν 2246 (CN), 1047, 1081 ($>S=O$) cm^{-1} ; ^1H NMR δ 2.40 - 2.60 (1H, m, -CHCN), 2.74 - 2.98 (2H, m, -SO-CH₂-), 3.10 - 3.28 (1H, m, -CHCN), 7.43 - 7.60 (4H, m, Ar); EIMS: m/z 213.5 (M^+ , 15%), 160.5 ($M\text{-CH}_2\text{=CH-CN}$, 25%), 159.5 ($M\text{-CH}_2\text{CH}_2\text{CN}$, 100%); HRMS: Found 213.00146. Calcd for C_9H_8NSCl 213.0015 (Cl^{35}); **3k**: 63% yield, IR ν 2246 (CN), 1056, 1093 ($>S=O$) cm^{-1} ; ^1H NMR δ 2.40 - 2.60 (1H, m, -CHCN), 2.76 - 2.98 (1H, m, -SO-CH-), 3.08 - 3.25 (1H, m, -SO-CH-), 3.30 - 3.50 (1H, m, -CHCN), 7.42 (1H, t, J = 7.5 Hz, Ar), 7.50 - 7.65 (2H, m, Ar), 7.77 (1H, d, J = 7.5 Hz, Ar); EIMS: m/z 258 (M^+ , 20%), 205 ($M\text{-CH}_2\text{=CH-CN}$, 29%), 204 ($M\text{-CH}_2\text{CH}_2\text{CN}$, 100%); HRMS: Found 256.9516. Calcd for C_9H_8NSBr 256.9510 (Br^{79}); **3l**: 83% yield, IR ν 2246 (CN), 1047, 1083 ($>S=O$) cm^{-1} ; ^1H NMR δ 2.38 - 2.60 (1H, m, -CHCN), 2.74 - 2.97 (2H, m, -SO-CH₂-), 3.06 - 3.25 (1H, m, -CHCN), 7.44 (2H, d, J = 7.5 Hz, AB system Ar) 7.65 (2H, d, J = 7.5 Hz, AB system Ar); EIMS: m/z 258 (M^+ , 7%), 205 ($M\text{-CH}_2\text{=CH-CN}$, 58%), 204 ($M\text{-CH}_2\text{CH}_2\text{CN}$, 29%); HRMS: Found 256.9518. Calcd for C_9H_8NSBr 256.9510 (Br^{79}); **3m**: 74% yield, IR ν 2246 (CN), 1040, 1068 ($>S=O$) cm^{-1} ; ^1H NMR δ 2.35 - 2.53 (1H, m, -CHCN), 2.78 - 3.08 (2H, m, -SO-CH₂-), 3.10 - 3.35 (1H, m, -CHCN), 7.37 - 7.70 (3H, m, Ar), 7.70 - 8.05 (3H, m, Ar), 8.15 (1H, s, Ar); EIMS: m/z 229 (M^+ , 13%), 176 ($M\text{-CH}_2\text{=CH-CN}$, 35%), 175 ($M\text{-CH}_2\text{CH}_2\text{CN}$, 100%); HRMS: Found 229.0571 Calcd for $C_{13}H_{11}NS$ 229.0561.

Typical experimental procedure for the formation of diaryldisulfides **6a-m** and diarylthiosulfonates **7a-m**:

The sulfoxide **3** (0.03 mol) in dry toluene (80 ml) was heated at reflux under nitrogen for 2h after which the solvent was evaporated and the residue showing two spots by TLC [1:5 ethyl acetate-petrol] was separated by flash chromatography to yield firstly **6** followed by **7. 6a** [12] and **7a** [12]. **6b**: 32% yield, oil, IR ν 1461, 1041, 1149 cm^{-1} ; ^1H NMR δ 2.50 (6H, s, 2x CH₃), 7.13 - 7.30 (6H, m, Ar),

7.55 - 7.65 (2H, d, $J = 7.50$ Hz, Ar); ^{13}C NMR δ 20.85, 125.38, 126.05, 130.96, 133.32, 142.08; EIMS: m/z 246 (M^+ , 83%), 123 ($\text{M} - \text{SC}_6\text{H}_4\text{-Me}$, 100%); HRMS: Calcd for $\text{C}_{14}\text{H}_{14}\text{S}_2$ 246.0537; Found 246.0530; **7b**: 30% yield, oil, IR ν 1315, 1145 cm^{-1} ; ^1H NMR δ 2.15 (3H, s, CH_3), 2.69 (3H, s, CH_3), 7.02 - 7.50 (8H, m, Ar); ^{13}C NMR δ 21.26, 21.64, 125.45, 126.10, 126.80, 128.25, 129.29, 131.24, 132.30, 133.20, 133.58, 137.65, 139.18, 142.10; EIMS: m/z 278 (M^+ , 50%), 123 ($\text{M} - \text{SC}_6\text{H}_4\text{-Me}$, 85%); HRMS: Calcd for $\text{C}_{14}\text{H}_{14}\text{O}_2\text{S}_2$ 278.04352; Found 278.04356; **6c**: 30% yield, oil, IR ν 1079, 1141 cm^{-1} ; ^1H NMR δ 2.34 (6H, s, 2x CH_3), 7.05 (2H, d, $J = 7.80$ Hz, Ar), 7.22 (2H, t, $J = 7.80$ Hz, Ar), 7.34 - 7.47 (4H, m, Ar); ^{13}C NMR δ 21.02, 124.22, 125.78, 126.75, 136.05, 140.59; EIMS: m/z 246 (M^+ , 100%), 123 ($\text{M} - \text{SC}_6\text{H}_4\text{-Me}$, 77%); HRMS: Found 246.0526. Calcd for $\text{C}_{14}\text{H}_{14}\text{S}_2$ 246.0537 **7c**: 24% yield, oil, IR ν 1318($-\text{SO}_2$), 1146 (S-O) cm^{-1} ; ^1H NMR δ 2.30 (3H, s, CH_3), 2.35 (3H, s, CH_3), 7.15 (2H, s, Ar), 7.20 - 7.45 (6H, m, Ar); ^{13}C NMR δ 21.42, 124.99, 128.28, 128.95, 129.49, 132.54, 133.89, 134.72, 137.41, 137.42, 139.71, 143.42, 143.05; EIMS: m/z 278 (M^+ , 47%), 139 ($\text{SO}_2\text{C}_6\text{H}_4\text{-Me}$, 100%); HRMS: Calcd for $\text{C}_{14}\text{H}_{14}\text{O}_2\text{S}_2$ 278.04352; Found 278.0447; **6d**: 35% yield, mp $45^\circ\text{C} - 47^\circ\text{C}$, IR ν 1340, 1116 cm^{-1} ; ^1H NMR δ 2.34 (6H, s, 2x CH_3), 7.13 (4H, d, $J = 7.80$ Hz, AB system Ar), 7.41 (4H, d, $J = 7.80$ Hz, AB system Ar), ^{13}C NMR δ 21.48, 128.47, 129.70, 133.85, 137.33; EIMS: m/z 246 (M^+ , 100%), 123 ($\text{M} - \text{SC}_6\text{H}_4\text{-Me}$, 86%); HRMS: Calcd for $\text{C}_{14}\text{H}_{14}\text{S}_2$ 246.0537; Found 246.05424; **7d**: 36% yield, mp $82^\circ\text{C} - 84^\circ\text{C}$, IR ν 1321 ($-\text{SO}_2$), 1137 (S-O) cm^{-1} ; ^1H NMR δ 2.38 (3H, s, CH_3), 2.43 (3H, s, CH_3), 7.07 - 7.30 (4H, m, Ar), 7.46 (2H, d, $J = 7.80$ Hz, Ar); ^{13}C NMR δ 21.33, 21.51, 124.44, 127.43, 129.25, 130.08, 136.32, 140.30, 141.93, 144.51; EIMS: m/z 278 (M^+ , 48%), 139 ($\text{SO}_2\text{C}_6\text{H}_4\text{-Me}$, 90%); HRMS: Calcd for $\text{C}_{14}\text{H}_{14}\text{O}_2\text{S}_2$ 278.04352; Found 278.0447; **6e**: 26% yield, mp $90^\circ\text{C} - 93^\circ\text{C}$, IR ν 1238 cm^{-1} ; ^1H NMR δ 3.91 (6H, s, 2x CH_3), 6.80 - 7.00 (4H, m, Ar), 7.13 - 7.30 (2H, m, Ar), 7.54 (2H, d, $J = 7.60$ Hz, Ar); ^{13}C NMR δ 56.25, 110.92, 121.70, 128.14, 138.68, 156.99; EIMS: m/z 278 (M^+ , 82%), 139 ($\text{SC}_6\text{H}_4\text{-OMe}$, 100%); HRMS: Calcd. for $\text{C}_{14}\text{H}_{14}\text{O}_2\text{S}_2$ 278.0435; Found 278.0440; **7e**: 35.5% yield, mp $113^\circ\text{C} - 115^\circ\text{C}$, IR ν 1247 ($-\text{SO}_2$), 1095, 1153 (S-O) cm^{-1} ; ^1H NMR δ 3.82 (3H, s, CH_3), 3.86 (3H, s, CH_3), 6.85 (4H, t, $J = 7.80$, Ar), 7.25 (2H, d, $J = 7.80$ Hz, Ar), 7.49 (2H, d, $J = 7.80$ Hz, Ar); ^{13}C NMR δ 55.82, 56.06, 114.32, 114.72, 115.26, 115.46, 130.14, 130.57, 138.15, 138.60, 162.57, 163.92; EIMS: m/z 310 (M^+ , 44%), 177 ($\text{SO}_2\text{C}_6\text{H}_4\text{-OMe}$, 22%), 155 ($\text{SOC}_6\text{H}_4\text{-OMe}$, 62%), 139 ($\text{SC}_6\text{H}_4\text{-OMe}$, 100%); HRMS: Calcd for $\text{C}_{14}\text{H}_{14}\text{O}_4\text{S}_2$ 310.0333; Found 310.0344; **6f**: 31% yield, oil, IR ν 1249, 1085, 1152 cm^{-1} ; ^1H NMR δ 3.79 (6H, s, 2x CH_3), 6.78 (2H, d, $J = 7.80$ Hz, Ar), 7.05 - 7.15 (4H, m, Ar), 7.23 (2H, d, $J = 7.8$ Hz, Ar); ^{13}C NMR δ 55.84, 111.09, 114.16, 119.47, 137.02, 161.00; EIMS: m/z 278 (M^+ , 41%), 139 ($\text{M-SC}_6\text{H}_4\text{-OMe}$, 100%); HRMS: Calcd for $\text{C}_{14}\text{H}_{14}\text{O}_2\text{S}_2$ 278.0435; Found 278.0439; **7f**: 45% yield, oil, IR ν 1286($-\text{SO}_2$), 1139, 1183 (S-O) cm^{-1} ; ^1H NMR δ 3.70 (6H, s, 2x OCH_3), 6.80 - 7.38 (8H, m, Ar); ^{13}C NMR δ 55.85, 111.20, 112.19, 114.09, 119.36, 120.72, 121.63, 130.10, 130.62, 133.50, 139.64, 160.06, 161.00; EIMS: m/z 310 (M^+ , 73%), 155 ($\text{SC}_6\text{H}_4\text{-OMe}$, 100%); HRMS: Calcd for $\text{C}_{14}\text{H}_{14}\text{O}_4\text{S}_2$ 310.0333; Found 310.0340; **6g**: 34% yield, oil, IR ν 1030, 1171 cm^{-1} ; ^1H NMR δ 3.81 (6H, s, 2x OCH_3), 6.84 (4H, d, $J = 7.75$ Hz, AB system

Ar), 7.41 (4H, d, $J = 7.75$ Hz, AB system Ar); ^{13}C NMR δ 55.90, 114.50, 128.54, 130.21, 157.10; EIMS: m/z 278 (M^+ , 95%), 139 ($\text{SC}_6\text{H}_4\text{-OMe}$, 100%); HRMS: Calcd. for $\text{C}_{14}\text{H}_{14}\text{O}_2\text{S}_2$ 278.0435; Found 278.0435; **7g**: 31% yield, oil, IR ν 1288 ($-\text{SO}_2$), 1170, 1032 (S-O) cm^{-1} ; ^1H NMR δ 3.75 (6H, s, 2x OCH_3), 7.50 (4H, d, $J = 7.80$ Hz, AB system Ar), 7.65 (4H, d, $J = 7.80$ Hz, AB system Ar); ^{13}C NMR δ 55.88, 114.64, 115.28, 124.90, 129.30, 130.37, 130.77, 130.81, 157.45, 165.72; EIMS: m/z 310 (M^+ , 60%), 155 ($\text{SC}_6\text{H}_4\text{-OMe}$, 100%); HRMS: Calcd. for $\text{C}_{14}\text{H}_{14}\text{O}_4\text{S}_2$ 310.0333; Found 310.0338; **6h**: 41% yield, $88^\circ\text{C} - 90^\circ\text{C}$, IR ν 1113, 1446 cm^{-1} ; ^1H NMR δ 7.12 - 7.30 (4H, m, Ar), 7.38 (2H, d, $J = 7.80$ Hz, Ar), 7.56 (2H, d, $J = 7.80$ Hz, Ar), 7.18 - 7.47 (4H, m, Ar), 7.48 - 7.70 (4H, m, Ar); ^{13}C NMR δ 127.17, 127.47, 127.73, 129.61, 131.80, 134.31; EIMS: m/z 286 (Cl^{35}) (M^+ , 90%), 143 ($\text{SC}_6\text{H}_4\text{-Cl}^{35}$, 85%); HRMS: Calcd. for $\text{C}_{12}\text{H}_8\text{S}_2\text{Cl}_2$ 285.9444 (Cl^{35}); Found 285.9455; **7h**: 37% yield, mp $157^\circ\text{C} - 160^\circ\text{C}$, IR ν 1329 ($-\text{SO}_2$), 1147 (S-O) cm^{-1} ; ^1H NMR δ 7.08 - 7.30 (4H, m, Ar), 7.38 (2H, d, $J = 7.80$ Hz, Ar), 7.56 (2H, d, $J = 7.80$ Hz, Ar); ^{13}C NMR δ 126.54, 127.60, 130.19, 130.91, 132.36, 133.10, 134.76, 139.72, 140.11, 140.21; EIMS: m/z 318 (Cl^{35}) (M^+ , 30%), 175 ($\text{SO}_2\text{C}_6\text{H}_4\text{-Cl}^{35}$, 35%), 143 ($\text{SC}_6\text{H}_4\text{-Cl}^{35}$, 68%), 159 ($\text{SOC}_6\text{H}_4\text{-Cl}^{35}$, 71%), 108 (100%); HRMS: Calcd. for $\text{C}_{12}\text{H}_8\text{O}_2\text{S}_2\text{Cl}_2$ 317.9343 (Cl^{35}); Found 317.9330; **6i**: 31% yield, oil, IR ν 1127, 1456 cm^{-1} ; ^1H NMR δ 7.17 - 7.30 (4H, m, Ar), 7.30 - 7.42 (2H, m, Ar), 7.49 (2H, s, Ar); ^{13}C NMR δ 125.33, 125.59, 129.15, 13.58, 133.50, 137.38; EIMS: m/z 286 (Cl^{35}) (M^+ , 100%), 143 ($\text{SC}_6\text{H}_4\text{-Cl}^{35}$, 78%); HRMS: Calcd. for $\text{C}_{12}\text{H}_8\text{S}_2\text{Cl}_2$ 285.9444 (Cl^{35}); Found 285.9455; **7i**: 32% yield, oil, IR ν 1294 ($-\text{SO}_2$), 1117 (S-O) cm^{-1} ; ^1H NMR δ 7.16 - 7.65 (8H, m, Ar); ^{13}C NMR δ 125.58, 126.39, 127.63, 127.61, 129.10, 130.71, 131.20, 133.61, 133.82, 133.93, 135.36, 140.10; EIMS: m/z 318 (Cl^{35}) (M^+ , 41%), 159 ($\text{SO}_2\text{C}_6\text{H}_4\text{-Cl}^{35}$, 100%), 143 ($\text{SC}_6\text{H}_4\text{-Cl}^{35}$, 64%); HRMS: Calcd. for $\text{C}_{12}\text{H}_8\text{O}_2\text{S}_2\text{Cl}_2$ 317.9343 (Cl^{35}); Found 317.9343; **6j**: 53% yield, mp $70 - 72^\circ\text{C}$, IR ν 1151 cm^{-1} ; ^1H NMR δ 7.28 (4H, d, $J = 7.80$ Hz, AB system Ar), 7.41 (4H, d, $J = 7.80$ Hz, AB system Ar), 7.28 (2H, t, $J = 7.80$ Hz, Ar), 7.48 - 7.64 (4H, m, Ar); ^{13}C NMR δ 129.15, 129.79, 133.51, 135.04; EIMS: m/z 286 (Cl^{35}) (M^+ , 86%), 143 ($\text{M-SC}_6\text{H}_4\text{-Cl}^{35}$, 100%); HRMS: Calcd. for $\text{C}_{12}\text{H}_8\text{S}_2\text{Cl}_2$ 285.9444 (Cl^{35}); Found 285.9451; **7j**: 26%, mp $131^\circ\text{C} - 135^\circ\text{C}$, IR ν 1322 ($-\text{SO}_2$), 1107 (S-O) cm^{-1} ; ^1H NMR δ 7.25 - 7.39 (4H, m, Ar), 7.42 (2H, d, $J = 7.80$ Hz, AB system Ar), 7.52 (2H, d, $J = 7.80$ Hz, Ar); ^{13}C NMR δ 129.25, 129.60, 130.22, 130.71, 137.98, 138.85, 140.87, 141.65; EIMS: m/z 318 (Cl^{35}) (M^+ , 50%), 175 ($\text{M-SC}_6\text{H}_4\text{-Cl}^{35}$, 85%), 143 ($\text{SC}_6\text{H}_4\text{-Cl}^{35}$, 83%), 111 (100%); HRMS: Calcd. for $\text{C}_{12}\text{H}_8\text{O}_2\text{S}_2\text{Cl}_2$ 317.9343 (Cl^{35}); Found 317.9345; **6k**: 43% yield, $91^\circ\text{C} - 93^\circ\text{C}$, IR ν 1357, 1151 cm^{-1} ; ^1H NMR δ 7.09 (2H, t, $J = 7.80$ Hz, Ar), 7.28 (2H, t, $J = 7.80$ Hz, Ar), 7.54 (4H, d, $J = 7.80$ Hz, Ar); ^{13}C NMR δ 121.00, 126.88, 127.83, 128.08, 132.80, 136.06; EIMS: m/z 378 (Br^{81}) (M^+ , 28%), 374 (Br^{79}) (M^+ , 25%), 189 ($\text{SC}_6\text{H}_4\text{-Br}^{81}$, 18%), 187 ($\text{SC}_6\text{H}_4\text{-Br}^{79}$, 17%); HRMS: Calcd. for $\text{C}_{12}\text{H}_8\text{S}_2\text{Br}_2$ 373.8434 (Br^{79}); Found 373.8445; **7k**: 35% yield, mp $138^\circ\text{C} - 140^\circ\text{C}$, IR ν 1326 ($-\text{SO}_2$), 1151 (S-O) cm^{-1} ; ^1H NMR δ 7.24 - 7.47 (4H, m, Ar), 7.57 (2H, t, $J = 7.80$ Hz, Ar), 7.71 (1H, d, $J = 7.80$ Hz, Ar), 7.80 (1H, d, $J = 7.80$ Hz, Ar); ^{13}C NMR δ 121.07, 121.25, 127.18, 128.20, 128.95, 131.07, 131.22, 132.93, 133.52, 134.56, 135.95, 141.82;

EIMS: m/z 410 (Br^{81}) (M^+ , 17%), 406 (Br^{79}) (M^+ , 15%), 221 ($\text{SO}_2\text{C}_6\text{H}_4\text{-Br}^{81}$, 18%), 219 ($\text{SO}_2\text{C}_6\text{H}_4\text{-Br}^{79}$, 19%), 205 ($\text{SOC}_6\text{H}_4\text{Br}^{81}$, 64%), 203 ($\text{SOC}_6\text{H}_4\text{Br}^{79}$, 61%), 108 (100%); HRMS: Calcd. for $\text{C}_{12}\text{H}_8\text{O}_2\text{S}_2\text{Br}_2$ 405.8332 (Br^{79}); Found 405.8344; **6l**: 57% yield, 87°C - 88°C , IR ν 1149 cm^{-1} ; ^1H NMR δ 7.34 (4H, d, J = 7.80 Hz, AB system Ar), 7.43 (4H, d, J = 7.80 Hz, AB system Ar); ^{13}C NMR δ 121.43, 129.28, 132.09, 135.62; EIMS: m/z 378 (Br^{81}) (M^+ , 52%), 374 (Br^{79}) (M^+ , 52%), 189 ($\text{SC}_6\text{H}_4\text{-Br}^{81}$, 60%), 187 ($\text{SC}_6\text{H}_4\text{-Br}^{79}$, 57%); HRMS: Calcd for $\text{C}_{12}\text{H}_8\text{S}_2\text{Br}_2$ 373.8434 (Br^{79}); Found 373.8439; **7l**: 28% yield, mp 105°C - 107°C , IR ν 1323 ($-\text{SO}_2$), 1142 (S-O) cm^{-1} ; ^1H NMR δ 7.24 (2H, d, J = 7.80 Hz, AB system, Ar), 7.44 (2H, d, J = 7.80 Hz, AB system, Ar), 7.52 (2H, d, J = 7.80 Hz, AB system Ar), 7.60 (2H, d, J = 7.80 Hz, AB system Ar); ^{13}C NMR δ 126.49, 126.88, 128.82, 129.06, 132.10, 132.78, 137.70, 141.75; EIMS: m/z 410 (Br^{81}) (M^+ , 38%), 406 (Br^{79}) (M^+ , 33%), 221 ($\text{SC}_6\text{H}_4\text{-Br}^{81}$, 52%), 199 ($\text{SC}_6\text{H}_4\text{-Br}^{79}$, 51%), 108 (100%); HRMS: Calcd for $\text{C}_{12}\text{H}_8\text{O}_2\text{S}_2\text{Br}_2$ 405.8332 (Br^{79}); Found 405.8321; **6m**: 46% yield; IR ν 1149 cm^{-1} ; ^1H NMR δ 7.54 (2H, d, J = 7.80 Hz, H-3), 7.60 (4H, m, H-6, H-7), 7.86 (2H, s, H-1), 7.98 (4H, m, H-4, H-8), 8.06 (2H, d, J = 7.80 Hz, H-4); ^{13}C NMR δ 126.58, 126.90, 128.09, 128.55, 129.30, 129.63, 129.68, 129.76; EIMS: m/z 318 (M^+ , 48%), 159 (SC_{10}H_7 , 59%), 115 (100%); HRMS: Calcd. for $\text{C}_{20}\text{H}_{14}\text{S}_2$ 318.0537; Found 318.0536; **7m**: 40% yield, IR ν 1323 ($-\text{SO}_2$), 1124 (S-O) cm^{-1} ; ^1H NMR δ 7.24 (1H, d, J = 7.80 Hz, H-3'), 7.60 (5H, m, H-1', H-6, H-6', H-7, H-7'), 7.85 (5H, m, H-4', H-5, H-5', H-8, H-8'), 8.15 (1H, d, J = 7.80 Hz, H-3), 8.38 (1H, d, J = 7.80 Hz, H-4), 8.85 (1H, s, H-1); ^{13}C NMR δ 126.05, 126.60, 126.88, 127.06, 128.10, 128.71, 129.30, 129.35, 129.41, 129.69, 129.80, 129.90, 130.2; EIMS: m/z 350 (M^+ , 10%), 159 (SC_{10}H_7 , 51%), 115 (100%); HRMS: Calcd for $\text{C}_{20}\text{H}_{14}\text{O}_2\text{S}_2$ 350.0435; Found 350.0436.

3.3. Microbiological Methods

Microorganisms: *E. coli* (JM 109) and *S. aureus* (SH1000) control strains were used to test antimicrobial activity. The series of compounds **6** and **7** were dissolved in DMSO to produce various concentrations which were refrigerated.

Inoculum: *E. coli* and *S. aureus* microorganisms were grown on Muller-Hinton Broth (MHB) for 24 hours at 37°C . Starting inocula were prepared by diluting overnight cultures in fresh MHB to a culture density of 1×10^6 cfu/ml. Minimum Inhibitory Concentrations (MIC) were determined according to the BSAC broth microdilution MIC methodology described by Andrews (2001).

4. Conclusion

We have shown how diarylthiosulfonates and diaryldisulfides, garlic-like organosulphur compounds can be conveniently synthesised in two steps in good yields. These compounds were tested for their antimicrobial properties against *Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Helicobacter pylori* and had been found to have good activity against *S. aureus* and *H. pylori* with no activity against the other two organisms. SAR analysis of the results has shown the presence of chloro- or bromo-groups in the 2-position of the

aromatic rings to be crucial for antimicrobial activities. By SAR analysis the most promising four active compounds were **6h**, **6k**, **7h** and **7k** against Gram-positive organisms *H. pylori* and *S. aureus*. These compounds offer the promising prospects for development into clinical candidates by further studies.

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Conflicts of Interest

These studies were supported by the BMRC and there is no conflict of interest to disclose.

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Graphical Abstract

